

Preliminary Amendment

Applicant(s): Danli WANG et al.

Serial No. 10/052,158

Confirmation No.: 1029

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For: FILM-FORMING COMPOSITIONS AND METHODS

Page 2 of 9

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that resist wash-off during surgery or exposure to fluids. Prior art attempts to improve the length of antiseptic activity through the use of film-forming polymers is described, for example, in U.S. Pat. Nos. 4,978,527 (Brink et al.) and 5,763,412 (Khan et al.). Many of these products also require an organic remover solution or lotion to get the prep off the skin. This is inconvenient for the clinician and requires significant extra time. - -

Please replace the paragraph beginning at page 16, line 29, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - Polymers prepared from these amine group-containing monomers in combination with long chain monomers may be pressure sensitive adhesives such as those described in Applicants' Assignee's copending U.S. Patent Application Serial No. 10/052,032, filed on even date herewith, entitled PRESSURE SENSITIVE ADHESIVES HAVING QUATERNARY AMMONIUM FUNCTIONALITY, ARTICLES, AND METHODS. - -

Please replace the paragraph beginning at page 18, line 29, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - Certain of the film-forming vinyl polymers of the present invention are themselves antimicrobial (i.e., they are inherently antimicrobial). U.S. Pat. No. 5,408,022 (Imazato et al.) teaches that certain quaternary amine functional polyacrylates have antimicrobial activity. In general, these include quaternary amine groups containing at least one organic moiety having at least 6 contiguous carbon atoms. Surprisingly, it has been discovered that acrylic polymers based on short chain quaternary ammonium groups (all 4 organic substituents having less than 6 contiguous carbon atoms) can also have significant antimicrobial activity if copolymerized with

monomers having alkyl groups having at least 8, and preferably at least 12 contiguous carbon atoms. Preferably, the alkyl groups have at most 22 carbon atoms, and more preferably at most 18 carbon atoms. For example, polyacrylate polymers based on trimethylaminoethyl methacrylate and 2-ethylhexyl acrylate show surprising antimicrobial activity. In addition, polyacrylate polymers based on trimethylaminoethyl methacrylate chloride salt and lauryl methacrylate appear to have even higher antimicrobial activity. In particular, polymers based on trimethylaminoethyl methacrylate chloride salt, lauryl methacrylate, and methyl methacrylate are particularly effective antimicrobial agents. - -

Please replace the paragraph beginning at page 22, line 16, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - Examples of antimicrobial agents include iodine and its complexed forms, which are commonly referred to as iodophors. Iodophors are complexes of elemental iodine or triiodide with certain carriers. These iodophors function to not only increase the iodine solubility but to reduce the level of free molecular iodine in solution and to provide a type of sustained release reservoir of iodine. Iodophors have been formed using carriers of polymers such as polyvinylpyrrolidone (PVP), copolymers of N-vinyl lactams with other unsaturated monomers such as, but not limited to, acrylates and acrylamides, various polyether glycols (PEGs) including polyether-containing surfactants such as nonylphenoethoxylates and the like, polyvinyl alcohols, polycarboxylic acids such as polyacrylic acid, polyacrylamides, polysaccharides such as dextrose, and the like. Also reported in U.S. Pat. No. 4,597,975 (Woodward et al.) are protonated amine oxide surfactant-triiodide complexes that are also suitable iodophors for use in the present invention. - -

Please replace the paragraph beginning at page 27, line 16, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - 6. *Alkyl Polyglucosides.* Alkyl polyglucosides, such as those described in U.S. Pat. No. 5,951,993 (Scholz et al.), starting at column 9, line 44, are compatible with the film-forming polymers of the present invention and may contribute to polymer stability. Examples include glucopon 425, which has a (C8-C16)alkyl chain length with an average chain length of 10.3 carbons and 1-4 glucose units. - -

Please replace the paragraph beginning at page 34, line 6, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - Suitable hydroxycarboxylic acid buffers include those described in Applicants' Assignee's copending U.S. Patent Application Serial No. 10/051,719, entitled ANTISEPTIC COMPOSITIONS AND METHODS. - -

Please replace the paragraph beginning at page 34, line 10, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - The hydroxycarboxylic acid buffers of the present invention preferably include beta- and alpha-hydroxy acids (BHAs, AHAs, respectively, collectively referred to as hydroxy acids (HAs)), their salts, lactones, and/or derivatives thereof. These may include mono-, di-, and tri-functional carboxylic acids. Particularly preferred are HAs having 1 or 2 hydroxyl groups and 1 or 2 carboxylic acid groups. Suitable HAs include, but are not limited to, lactic acid, malic acid,

citric acid, 2-hydroxybutanoic acid, 3-hydroxybutanoic acid, mandelic acid, gluconic acid, tartaric acid, salicylic acid, as well as derivatives thereof (e.g., compounds substituted with hydroxyls, phenyl groups, hydroxyphenyl groups, alkyl groups, halogens, as well as combinations thereof)). Preferred HAs include lactic acid, malic acid, and citric acid. These acids may be in D, L, or DL form and may be present as free acids, lactones, or salts thereof. Other suitable HAs are described in U.S. Pat. No. 5,665,776 (Yu et al.). The preferred HAs for use with iodine and in particular with povidone-iodine are lactic and malic acid. Various combinations of hydroxycarboxylic acids can be used if desired. - -

Please replace the paragraph beginning at page 35, line 14, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - In addition to hydroxycarboxylic acid buffers, a variety of other ingredients may be added to the compositions of the present invention for desired effect. These include, but are not limited to, skin emollients and humectants such as those described in U.S. Pat. No. 5,951,993 (Scholz et al.), fragrances, colorants, tackifiers, plasticizers, etc. - -

Please replace the paragraph beginning at page 50, line 28, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - Compositions were evaluated for their potential for eye irritation compared to commercially available antiseptics: BETADINE Surgical Scrub (7.5% povidone- iodine) and BETADINE Sterile Ophthalmic Prep Solution (5% povidone-iodine). The test involved instilling into the eyes of adult New Zealand White albino rabbits weighing 2.0-3.5 Kg of either sex. Proper husbandry of the animals prior to testing is ensured including clean housing, high fiber

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Page 6 of 9

rabbit diets (No. 5326 Purina Mills, Inc.), proper clean watering, proper environmental control (16°C-22°C, 30%-70% relative humidity, and a 12 hour light/12 hour dark cycle). All animals were acclimated for at least 5 days and were given various cage-enrichment devices. Eyes were examined using sodium fluorescein dye on the day before the test material administration to ensure no sign of corneal injury or eye abnormality was present. Each test material was administered to three rabbits with 0.1 mL of undiluted test material/eye for two consecutive days. The eyelids were gently held together for 1 second before releasing to prevent loss of the material. The eyes of the rabbits remained unflushed for approximately 24 hours following instillation of the test material. The right eye of each animal was treated while the left eye remained untreated as a control. The eyes were examined for ocular irritation at 1, 4, 24, 48, and 72 hours after their respective treatment. Additional observations were made at 96 and 120 hours if irritation was present at 72 hours. Sodium Fluorescein was used to aide in revealing possible corneal injury for each animal beginning with the 24-hour examination and each continuing examination until a negative response was attained. Irritation was scored using the Ocular Draize Technique (J. H. Draize: "Dermal Toxicity, " *Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics*, Association of Food and Drug Officials of the U.S., 1959, pages 46-59) with some modification. The maximum total score for these examples was the sum of scores obtained only from the conjunctivae. Total maximum score possible is 60 (20 per eye times three eyes). Notes were made with respect to the Cornea opacity, but this was not included in the scoring. - -

Please replace the paragraph beginning at page 92, line 14, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

- - The composition of Example 14 was absorbed to saturation in gauze and applied to the inner forearm of a volunteer by simply painting the formulation on the arm 3 times in a

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Page 7 of 9

continuous circular motion. The prep was allowed to stay in place for at least 2 minutes after which time a glass-sampling cylinder with an area of 5.04 cm² was pressed to the skin over the prep. Into this sampling cylinder was dispensed 2.5 mL sterile sampling solution. The sampling solution was mixed thoroughly in the glass cylinder on the arm using a TEFLON policeman for 1 minute making certain to rub over the skin in the entire area within the cylinder. The solution was removed and placed into a sterile test tube using a pipet. A second aliquot of 2.5 mL of sampling solution was added to the cylinder and the process repeated. The two 2.5-mL aliquots were combined into one tube. To the test tube was added 50 microliters of *Staphylococcus epidermidis* ATCC Number 12228 at a concentration sufficient to yield a diluted concentration in the combined sampling solution of *Staphylococcus epidermidis* ATCC Number 12228 at a concentration sufficient to yield a diluted concentration in the combined sampling solution of approximately 20-50 colony forming units (CFU)/mL Control samples of both the Standard Sterile Solution (SSS) and Modified Sterile Solution (MSS) were also run. In one set of controls the bacteria were inoculated directly into SSS and MSS as well as into Butterfield's phosphate buffered water (PBW) (*Journal of Bacteriology*, Vol. 23, No. 355, (1932)) to determine if the sampling solutions were toxic to the bacteria. - -